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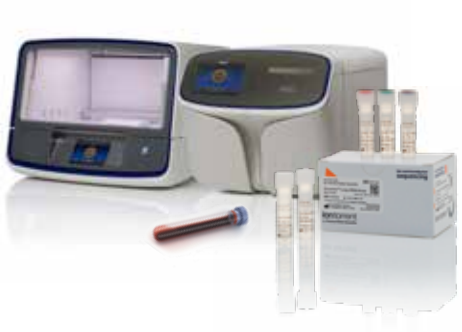
Comprehensive liquid biopsy analysis with only one tube of blood

Relevant insights from DNA, RNA, and all classes of variants



The Ion Torrent™ Oncomine™ Pan-Cancer Cell-Free Assay is a targeted next-generation sequencing (NGS) assay that delivers current, relevant insights for oncogenes associated with more than 18 different cancer types. Through simultaneous multibiomarker analysis of DNA and RNA from just one tube of blood, results are now only three days away.

- **Multiple biomarkers from one blood sample**—this complementary, noninvasive option to traditional tissue biopsies only requires one tube of blood for detection of variants across 52 oncogenes that are associated with 18 different cancer types
- **One assay, two programs**—two distinct programs are available for initial evaluation of the Oncomine Pan-Cancer Cell-Free Assay, or for potential adoption into your menu; these programs are available through Life Technologies Clinical Services Lab (lifelabdx.com or toll-free 1.888.734.8588)
- **One streamlined workflow**—go from blood sample to variant report in three days
- **Established performance**—tissue orthogonal concordance was conducted on plasma samples with corresponding solid tumor molecular characterization; reported concordance for SNVs and CNVs at >99%; key confirmed alterations observed in clinical samples include *EGFR* p.E746_A750del, *EGFR* p.T790M, *EGFR* p.G719S, *KRAS* G12/13, *NRAS* codon 61, *ERBB2* amp, *EGFR* amp

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Table 1. Gene targets included in Oncomine Pan-Cancer Cell-Free Assay.

Hotspot genes			Tumor suppressor genes	Copy number genes	Gene fusions
AKT1	*FGFR2*	*MET*	*APC*	*CCND1*	*ALK*
ALK	*FGFR3*	*MTOR*	*FBXW7*	*CCND2*	*BRAF*
AR	*FGFR4*	*NRAS*	*PTEN*	*CCND3*	*ERG*
ARAF	*FLT3*	*NTRK1*	*TP53*	*CDK4*	*ETV1*
BRAF	*GNA11*	*NTRK3*		*CDK6*	*FGFR1*
CHEK2	*GNAQ*	*PDGFRA*		*EGFR*	*FGFR2*
CTNNB1	*GNAS*	*PIK3CA*		*ERBB2*	*FGFR3*
DDR2	*HRAS*	*RAF1*		*FGFR1*	*MET*
EGFR	*IDH1*	*RET*		*FGFR2*	*NTRK1*
ERBB2	*IDH2*	*ROS1*		*FGFR3*	*NTRK3*
ERBB3	*KIT*	*SF3B1*		*MET*	*RET*
ESR1	*KRAS*	*SMAD4*		*MYC*	*ROS1*
FGFR1	*MAP2K1*	*SMO*			
	MAP2K2				

Table 2. 18 cancer types included in Oncomine Pan-Cancer Cell-Free Assay.

Cancer types	Top 10 genes ranked by mutation frequency
Bladder	*TP53, PIK3CA, FGFR3, HRAS, ERBB2, KRAS, CTNNB1, BRAF, NRAS, FBXW7*
Brain and CNS	*TP53, IDH1, PIK3CA, EGFR, CHEK2, ALK, CTNNB1, BRAF, PTEN, PDGFRA*
Breast	*PIK3CA, TP53, ERBB2, PTEN, SF3B1, AKT1, ERBB3, ESR1, KRAS, FGFR2*
Cervical	*PIK3CA, FBXW7, TP53, KRAS, ERBB2, PTEN, ERBB3, MTOR, CTNNB1, SMAD4*
Colorectal	*PIK3CA, FBXW7, TP53, KRAS, ERBB2, PTEN, ERBB3, MTOR, CTNNB1, SMAD4*
Endometrial	*PIK3CA, TP53, CTNNB1, PTEN, KRAS, FGFR2, FBXW7, MTOR, NRAS, ERBB2*
Esophageal	*TP53, PIK3CA, SMAD4, FBXW7, KRAS, ERBB2, APC, CTNNB1, PTEN, SMO*
Gastric	*TP53, PIK3CA, KRAS, FBXW7, ERBB3, ERBB2, SMAD4, CTNNB1, APC, MAP2K1*
Head and neck	*TP53, PIK3CA, HRAS, PTEN, FBXW7, RET, KRAS, FGFR3, BRAF, ERBB2*
Kidney	*TP53, MTOR, CHEK2, PIK3CA, PTEN, MET, FGFR3, EGFR, KRAS, SF3B1*
Liver	*CTNNB1, TP53, PIK3CA, KRAS, PTEN, KIT, IDH1, GNAS, APC, FGFR2*
Lung	*TP53, KRAS, EGFR, PIK3CA, BRAF, NRAS, PTEN, FBXW7, APC, CTNNB1*
Melanoma	*BRAF, NRAS, TP53, MAP2K1, CTNNB1, GNA11, PTEN, IDH1, KIT, GNAQ*
Ovarian	*TP53, PIK3CA, KRAS, EGFR, CTNNB1, CHEK2, ERBB2, MET, FBXW7, NRAS*
Pancreatic	*KRAS, TP53, SMAD4, APC, GNAS, CTNNB1, SF3B1, PIK3CA, BRAF, FGFR1*
Prostate	*TP53, PIK3CA, CTNNB1, AR, CHEK2, APC, PTEN, IDH1, AKT1, BRAF*
Sarcoma	*TP53, IDH1, NRAS, PIK3CA, KRAS, FGFR4, ERBB2, IDH2, HRAS, CTNNB1*
Thyroid	*BRAF, NRAS, HRAS, RET, TP53, KRAS, PIK3CA, AKT1, GNAS, CCND1*

Next-generation sequencing (NGS) workflow—from sample to report

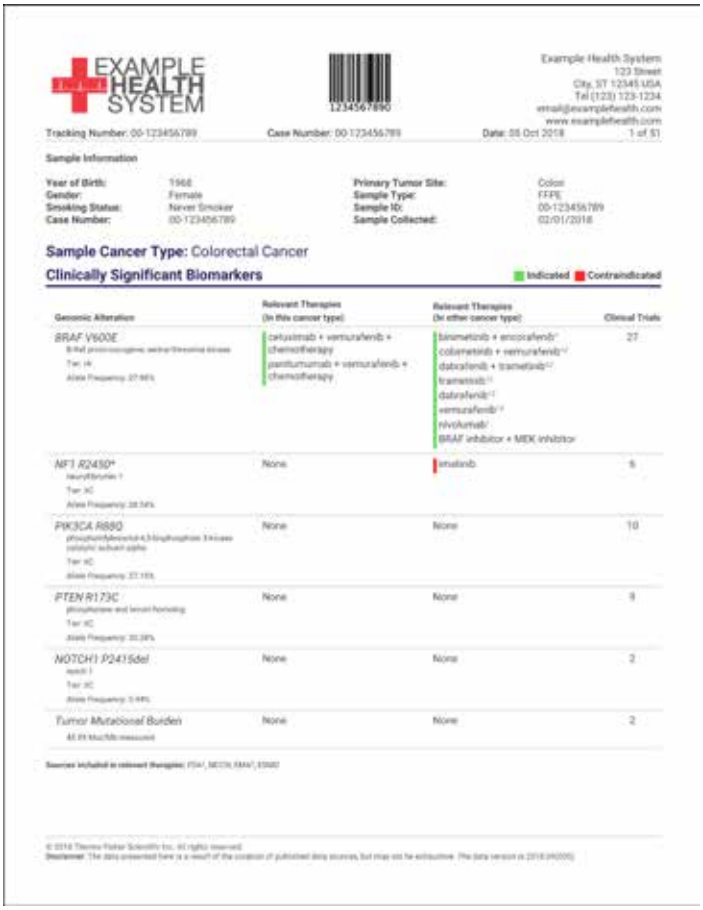
Sample prep	Sequencing	Analytics
• Cell-free isolation (Applied Biosystems™ MagMAX™ cell-free isolation kits)	• High-throughput semiconductor sequencing (Ion GeneStudio™ S5 System Series)	• Variant caller for optimized analysis (Torrent Suite™ Software, Ion Reporter™ Software)
• Library preparation (Oncomine Pan-Cancer Cell-Free Assay)		• Labels, guidelines, and global clinical trials (Ion Torrent™ Oncomine™ Reporter)
• Template preparation (Ion Chef™ Instrument)		

A comprehensive liquid biopsy NGS workflow for streamlined detection and analysis of variants from 52 oncogenes (Table 1) that are associated with 18 different cancer types (Table 2). Receive a report in three days with relevant insights that may provide guidance regarding future treatment decisions.

Next-generation sequencing (NGS) workflow—optimized for operational efficiency from sample to report, the NGS workflow for the Oncomine Pan-Cancer Cell Free Assay consists of three key steps, enabling you to go from blood sample to report in three days. During sample preparation, cell-free nucleic acids are extracted, enriched, and amplified. These amplicon-based libraries are then assembled overnight before targeted resequencing. Our integrated informatics solution then takes you from variant caller to a finished report that provides contextual insights about sample-specific variants and their use with respect to labels, guidelines, and current global clinical trials.

Strong concordance with tissue samples enables confidence in your liquid biopsy results

Tissue orthogonal concordance was evaluated on plasma samples with corresponding solid tumor molecular characterization. Reported concordance for SNVs and CNVs were shown to be >99%. Key confirmed alterations observed in samples include *EGFR* p.E746_A750del, *EGFR* p.T790M, *EGFR* p.G719S, *KRAS* G12/13, *NRAS* codon 61, *ERBB2* amp, and *EGFR* amp.


EXAMPLE HEALTH SYSTEM

Sample Cancer Type: Colorectal Cancer

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
BRAF V600E	cetuximab + vemurafenib + chemotherapy panitumumab + vemurafenib + chemotherapy	binimetinib + encorafenib colorectinib + vemurafenib dabrafenib + trametinib trametinib dabrafenib vemurafenib nivolumab BRAF inhibitor + MEK inhibitor	27
*NF1 R2450**	None	erlotinib	5
PIK3CA R88Q	None	None	10
PTEN R173C	None	None	9
NOTCH1 P2415del	None	None	2
Tumor Mutational Burden	None	None	2

Sample report from Oncomine Reporter links variant data to current labels, guidelines, and clinical trials. Information is provided in an easy-to-consume format.

Performance data of the Oncomine Pan-Cancer Cell-Free Assay

Validation item	SNV/indel	CNV	Fusion
Analytical sensitivity	• >99.9% at 0.5% allele fraction • 80% at 0.1% allele fraction	>99% at >1.35 fold amplification	>99% at 0.4% fusion fraction
Analytical specificity	>99%	>99%	>99%
Analytical accuracy	>99%	>99%	>99%
Precision within run	98%	>99%	>99%
Precision across runs	99%	>99%	>99%
Tissue concordance	>99% for informative variants	>99% for informative variants	N/A

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Two programs to get you started

If your laboratory is interested in a trial evaluation of your samples using the Oncomine Pan-Cancer Cell-Free Assay, sequencing and analysis is available through the Proof-of-Principle program.

If your laboratory is interested in validating and incorporating the Oncomine Pan-Cancer Cell-Free Assay into your menu, analytical validation support is also available.

Both programs are supported and executed by our CLIA-certified, CAP-accredited clinical services lab facility, Life Technologies Clinical Services Lab (LTCSL). LTCSL can help pharma and other customers find comprehensive, accurate answers. They specialize in developing oncology molecular assays for pharmaceutical clients with small, challenging samples.

Life Technologies Clinical Services Lab offers a comprehensive end-to-end oncology workflow, including histology, pathology, and NGS. They also provide custom assay development and analytical validation services to pharma customers using multiple technology platforms (qPCR, Sanger sequencing, and NGS), custom design, and existing analytically validated panels. For more information or to get started with their programs, please visit lifelabdx.com or call toll free 1.888.734.8588.

Proof-of-Principle (POP) program

The POP program is designed for customers interested in evaluating the Oncomine Pan-Cancer Cell-Free Assay with their own research samples. A small batch will be run on our NGS workflow, and a report with optional raw data will be provided back to you.

Sample requirements for the POP program

- The specimen must be NSCLC
- Plasma obtained from two 10 mL K_2EDTA tubes (lavender top) at a minimum
- Whole blood should be processed within 6 hours post-collection
- Whole blood samples should be spun for 10 minutes at 1,000–2,000 x *g* in a refrigerated centrifuge

Plasma should be separated from whole blood after centrifugation is completed, taking care not to disturb the buffy coat.

Analytical validation support

This program is designed for customers interested in validating and incorporating the Oncomine Pan-Cancer Cell-Free Assay into their menu. During the validation period, services will be provided to the customer to help minimize or potentially eliminate downtime as a result of the analytical validation efforts.

For more information, visit **thermofisher.com/cfna-assays**

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